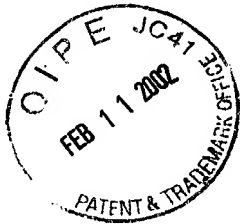


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PATENT  
ATTORNEY DOCKET NO. JHU1180-1

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicants: David Sidransky      Art Unit: 1655  
Application No.: 09/420,433      Examiner: D. Johannsen  
Filed: October 12, 1999  
Title: NUCLEIC ACID MUTATION DETECTION IN HISTOLOGIC TISSUE

Commissioner for Patents  
Washington, DC 20231

**RECEIVED**

FEB 19 2002

TECH CENTER 1600/2900

**TRANSMITTAL SHEET**

Sir:

Transmitted herewith for the above-identified application please find:

1. Response to the Office Communication mailed November 19, 2001 (5 pages);
2. Petition for One (1) Month Extension of Time (2 pages);
3. Change of Attorney Address
4. Check Nos. 499233 and 499416 totaling \$110.00, each in the amount of \$55.00;  
and
5. Return Receipt Postcard.

CERTIFICATION UNDER 37 CFR §1.8	
I hereby certify that the documents referred to as enclosed herein are being deposited with the United States Postal Service as first class mail on this date, January 18, 2002, in an envelope addressed to: Commissioner for Patents, Washington, D.C. 20231.	
Aldon Griffis (Name of Person Mailing Paper)	
Aldon Griffis (Signature)	January 18, 2002 (Date)

In re Application of:  
David Sidransky  
Application No.: 09/420,433  
Filed: October 12, 1999  
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PATENT  
Attorney Docket No.: JHU1180-1

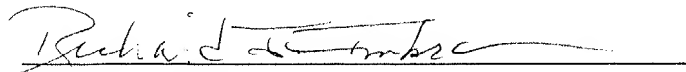
The Fee for this Response is calculated as follows:

For	Claims Remaining After Amendment	Highest Number Previously Paid For	Extra Claims	Small Entity Rate	Large Entity Rate	Calculations
Total Claims	27	27	0	x \$09	x \$18	\$ .00
Independent Claims	6	6	0	x \$42	x \$84	\$ .00
Multiple Claims	-	-		\$140	\$280	\$ .00
Basic Filing Fee				\$370	\$740	\$ .00
					TOTAL FEE	\$ .00

Enclosed are Check Nos. 499233 and 499416 totaling \$110.00, each in the amount of \$55.00; which consists of the fee for one (1) month extension of time. The Commissioner is hereby authorized to charge any other fees associated with the filing submitted herewith, or credit any overpayments to Deposit Account No. 50-1355. A duplicate copy of this sheet is enclosed.

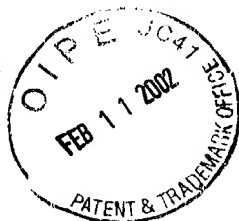
Respectfully submitted,

Date: January 18, 2002

  
Richard J. Imbra  
Registration No. 37,643  
Telephone: (858) 677-1496  
Facsimile: (858) 677-1465

**USPTO Customer Number 28213**  
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: David Sidransky Art Unit: 1655  
Application No.: 09/420,433 Examiner D. Johannsen  
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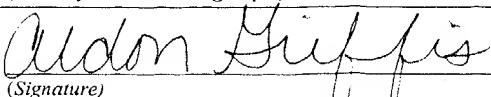
**RESPONSE TO THE SPECIES ELECTION REQUIREMENT**

Sir:

Responsive to the Office Action mailed November 19, 2001 (Paper No. 14), in which a species election was requested, reconsideration of the species election requirement in view of the following remarks is respectfully requested.

Claims 1 to 27 are pending. It is stated in the Office Action that the claims are directed to patentably distinct species, which are set forth as follows:

- a) methods requiring detection or a mutant/neoplastic target nucleic acid in a tumor margin tissue specimen;
- b) methods requiring detection or a mutant/neoplastic target nucleic acid in a lymph node tissue specimen; and
- c) methods requiring detection or a mutant/neoplastic target nucleic acid in a surgical margin adjacent to an excised tumor.

CERTIFICATION UNDER 37 CFR §1.8	
I hereby certify that the documents referred to as enclosed herein are being deposited with the United States Postal Service as first class mail on this date, <b>January 18, 2002</b> , in an envelope addressed to: Commissioner for Patents, Washington, D.C. 20231.	
Aldon Griffis (Name of Person Mailing Paper)	
 (Signature)	January 18, 2002 (Date)

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David Sidransky  
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Although the species election is traversed for the reasons set forth below, Applicant nevertheless provisionally elects the species set forth by the Examiner as "c), methods requiring detection or a mutant/neoplastic target nucleic acid in a surgical margin adjacent to an excised tumor" in order to be fully responsive to the Office Action. Applicant points out that claims 12 to 17 read on the elected species, as does claim 18, which the Examiner has indicated is generic. Applicant further submits that the elected species reads, in part, on claims 1 to 11 and 19, which refer to a "tumor margin tissue specimen", because, for example, a "surgical margin adjacent to an excised tumor" can comprise primary tumor tissue in the surgical site (see below).

The species election is traversed for the following reasons. First, the subject application is a "continued prosecution application" (CPA) and the subject matter set forth as species a) to c) above was pending prior to filing the request for a CPA. However, no request for a species election was previously set forth, even though the species as set forth in the present Office Action were encompassed within the claims. For example, well before Applicant's request for the present CPA, claim 1 was directed to methods relating to "tumor margin" or "lymph node" and claim 12 was directed to methods relating to "a surgical margin adjacent to [an] excised tumor" (see, for example, Applicant's Amendment filed December 21, 2000, in response to the Office Action mailed June 22, 2000). However, no species election was requested with respect to the subject matter of the previously pending claims.

Applicant's submit that the requirement to elect a species at such an advanced stage in the prosecution of the claimed subject matter is improper because the requirement could have been made much earlier in the prosecution. Furthermore, the requirement for a species election at this stage of the prosecution is inconsistent with the previous prosecution and, therefore, creates an undue burden on the Applicant by introducing uncertainty, including a potential for unexpected significant costs if, for example, it is later found that one or more of the "species" must be

prosecuted in a separate patent application. For this reason, it is requested that the requirement for a species election be withdrawn.

The requirement for a species election also is traversed because, while the species set forth as a), b) and c) by the Examiner are independent and patentably distinct, the claimed subject matter is related by a "commonality of operation, function and effect" (see MPEP § 806.04(e)). More specifically, Applicant's invention is based, in part, on the discovery that a mutant target nucleic acid molecule can be detected in tissue, including tumor margin, surgical margin adjacent to a tumor, and lymph node, that otherwise appears to be histologically normal, and the claimed methods all require substantially similar steps including, for example, examining a specimen that appears histologically normal for the presence of a mutant nucleotide sequence. As such, it is submitted that the requirement to elect a species is improper and should be withdrawn pursuant to MPEP § 806.04(e) because each of the "species" is related in that it appears histologically normal and because the methods to be practiced are substantially identical with respect to each of the species.

The species election requirement also is traversed particularly with respect to the species set forth as a) "tumor margin" and c) "surgical margin". More specifically, it would not appear that separate searches would need to be performed because, regardless of whether a tumor is present or whether the tumor has been surgically excised, the specimen being obtained comprises tissue that is not part of the tumor and histologically appears to be normal. No objective reasoning is provided in the Office Action to support the position that these specimens should or need be examined separately. As such, Applicant is uncertain as to the basis for separating the specimens set forth as species a) and c) based on what is present 'external' to the specimen (i.e., a tumor or tissue remaining after removal of the tumor) because what is (a tumor) or was (a surgical margin) present in the vicinity of the specimen would not appear to be relevant to the

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specimen itself or to the examination of methods for examining such specimens as set forth in the claims.

Furthermore, Applicant points out that a "tumor margin tissue specimen" (species a)) can encompass a "surgical margin adjacent to an excised tumor" (species b)) and, vice versa, that a "surgical margin adjacent to an excised tumor" can comprise primary tumor tissue at the site of the surgery because surgical excision of a tumor may not be sufficiently exact to remove all of a tumor and, therefore, primary tumor tissue can be present following a surgical excision. As such, it is submitted that the division of species a) and c) is artificial and, if maintained, would result in incomplete examination of the claimed subject matter. Accordingly, it is respectfully requested that at least the species set forth as a) and c) be rejoined for examination or, alternatively, that objective reasoning in support of the request for an election be provided.

In summary, it is submitted that the species election requirement is improper in view of the previous prosecution and because the species as set forth are related by a commonality of operation, function and effect. As such, it is respectfully requested that the species election be removed and that all of the claimed subject matter be examined together. Furthermore, even if the species election is maintained with respect to species a), b) and c), it is submitted that the subject matter of species a) and c) is so related that a division of this subject matter into separate species is artificial and that it would not be possible to perform a complete and thorough examination of one of the species without also examining the other species. Accordingly, it is respectfully requested that at least the species set forth as species a) and species c) be examined together.

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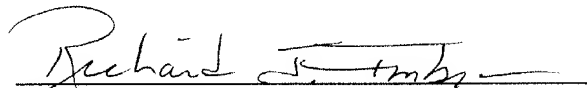
PATENT  
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Notwithstanding the above remarks, species c), directed to methods requiring detection or a mutant/neoplastic target nucleic acid in a surgical margin adjacent to an excised tumor is provisionally elected for examination. The Examiner is invited to contact the undersigned if there are any questions relating to the subject application.

Please charge any additional fees, or made any credits, to Deposit Account No. 50-1355.

Respectfully submitted,

Date: January 18, 2002



Richard J. Imbra  
Reg. No. 37,643  
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